Glaucoma pathology: an eye on the brain

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Article first published online: 20 AUG 2014

DOI: 10.1111/j.1755-3768.2014.3421.x

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Abstract

Purpose Glaucoma is a group of optic neuropathies characterized by loss of retinal ganglion cells (RGC). Since ocular hypertension (OHT) is one of the main risk factors, current therapies are merely based on lowering eye pressure. As a subset of treated patients continue losing vision, more research into the pathological mechanisms underlying glaucoma is needed in order to develop novel therapeutic strategies. Here, we studied the impact of OHT on the main visual areas in the mouse brain: superior colliculus (SC) and primary visual cortex (V1).

Methods Temporary monocular hypertension (5 days) was induced in mice by lasering the episcleral and perilimbal vessels. The impact on the retina and its target areas was examined via immunohistochemistry (Brn3a, VGluT2 and GFAP). Alterations in neuronal activity in V1 were assessed via in situ hybridization for zif268.

Results Transient OHT resulted in diffuse and sectorial RGC death. In the SC contralateral to the OHT eye, we detected a strong decrease in synaptic connections at 1 week after lasering, which was retinotopically linked to RGC degeneration patterns in the retina. Similar retinotopic dropouts were discerned in activity patterns of V1 at 1 week post lasering, while V1 activity resumed 3 weeks later. In the SC, however, no recovery of synapse density was observed and inflammation was not resolved at 4 weeks post lasering. Nevertheless, SC neurons appeared healthy and cell density and cell morphology looked normal.

Conclusion Besides RGC death, OHT also induces loss of synaptic connections and neuronal activity in visual brain centers, accompanied by extensive immune responses. This stresses the importance of including the whole visual system in glaucoma research.